vertebrate Hox genes, this property may partially underlie their highly compact arrangement within the Hox clusters.

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Program/Abstract # 528

The Wnt/bcatenin target, Mesogenin1 (Msgn1), directly regulates the Notch pathway during mammalian somitogensis

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The Wnt family of secreted signaling molecules are important regulators of stem cell fates during normal development and disease. One of the Wnt molecules, Wnt3a is required both for the maintenance of the mesoderm progenitors and for their subsequent differentiation into somites. A dynamic Notch-centered molecular oscillator governs the rhythmic formation of somites and lies downstream of Wnt3a, however the underlying mechanisms are not well understood. In a microarray screen of wildtype and Wnt3a mutant embryos, we identified the bHLH transcription factor, Mesogenin1 (Msgn1), as a differentially expressed gene. Msgn1 mutants show defects in somitogenesis leading to a lack of trunk skeletal muscles, vertebra and ribs. To study the molecular and cellular function of Msgn1 in ESC, we have generated inducible gain-of-function ESC that overexpress Msgn1 and have shown that Msgn1 promotes the formation of paraxial mesoderm progenitors. Integration of genome-wide microarray and Chromatin immunoprecipitation (CHIP)-seq studies of these ESCs led to the discovery that Msgn1 directly activates genes involved in the Notch centered segmentation clock during somitogenesis. Msgn1 upregulated the expression of multiple Notch pathway genes including Dll1, Dll3, Notch1, Nrarp and Lfng and bound directly to their regulatory elements. Moreover, expression analyses in Msgn1 null mutants revealed that these Notch pathway genes required Msgn1 for their proper expression in vivo. Our studies demonstrate that Msgn1 is a critical effector of the Wnt pathway during mammalian somitogenesis, mediating crosstalk between the Wnt and Notch pathways.

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Program/Abstract # 531

Role of SoxD proteins in regulating SoxE function during neural crest development

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SoxE family transcription factors (Sox8, Sox9, and Sox10) are essential neural crest regulatory factors. They act reiteratively throughout neural crest development to promote the formation, maintenance and differentiation of neural crest cells. With respect to neural crest derivatives, SoxE factors are essential for the proper development of craniofacial cartilage, melanocytes, and peripheral glia. Interestingly, SoxE factors induce the formation of derivatives in a context-dependent manner. In order to determine how SoxE factors can differentially regulate the formation of neural crest derivatives, we are investigating the role of a related group of Sox family proteins, the SoxD factors (Sox5, Sox6, and Sox13), which are known to modulate SoxE function. SoxD proteins can enhance the ability of SoxE proteins to promote chondrocyte differentiation but inhibit their ability to induce melanocyte and glial cell fates. We have characterized the expression, requirement, and function of the SoxD factor, Sox5 in Xenopus. We show that Sox5 is expressed in neural crest precursor cells, as well as in mesoderm, and pre-placodal ectoderm during *Xenopus laevis* development. Morpholino mediated knockdown of Sox5 causes a reduction in neural crest marker expression, suggesting that Sox5 is required for neural crest development. We examine the role of SoxD factors in modulating SoxE function during distinct stages of neural crest development, including its effects on DNA binding, protein-protein interactions and the activation or repression of target genes.

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SUMO regulation of SoxE factors during neural crest development

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A growing number of transcriptional regulatory proteins have been found to be modified by the small ubiquitin like modifier, SUMO. Post translational modification by SUMO may be one means by which transcriptional regulatory factors that play context dependent roles in multiple processes can be regulated such that they direct the appropriate cellular and developmental outcomes. In early vertebrate embryos, SUMOylation of transcription factors of the SoxE family has a dramatic affect on their function, inhibiting their neural crest inducing activity and promoting ear formation. Here we provide mechanistic insight into how SUMO modification affects SoxE function as well as how SUMOylation of SoxE factors is regulated. We show that SUMO has a dramatic affect on the ability of SoxE transcription factors to recruit transcriptional co-regulator factors, displacing the binding of CBP and p300 while promoting the recruitment of co-repressor Grg4. These data suggest that SoxE transcription factors can function as transcriptional repressors in a SUMO-dependent fashion. We also demonstrate that upstream molecules such as BMP and PIAS modulate the SUMOylation of SoxE factors. These results shed light on the control of SoxE SUMOylation during neural crest development, and also provide insights into the mechanisms of SUMO-dependant transcriptional regulation more generally.

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